

Amendments to the Specification:

Please insert the following paragraph on page 1 before the "Background of the Invention":

Cross Reference to Related Applications

This application is a continuation of U.S. application Serial No. 09/290,029, filed April 9, 1999, pending, which is incorporated herein by reference.

Please replace the paragraph beginning on page 4 at line 3 with the following amended paragraph:

There are two main categories of helper cell subtypes: Th1 and Th2. A particular naive CD4 T cell differentiates into a cell of one or the other subtype as part of its activation process; which subtype it selects is determined by which cytokines are present in the environment of the T cell during its activation. In particular, a Th1 response is selectively induced when activated T cells encounter antigen in the presence of IL-12, IL-18, IFN α , and/or IFN γ ; a Th2 response is induced when activated T cells encounter antigen in the presence of IL-4.

Please replace the paragraph beginning on page 8 at line 21 with the following amended paragraph:

"Antigen": means (i) any compound that elicits an immune response; and/or (ii) any compound that binds to a T cell receptor or to an antibody produced by a B-cell. Furthermore, for the purposes of the present invention the following subsets subset of antigens is are specifically defined: an "allergen" is an antigen that (i) elicits an IgE response in an individual; and/or (ii) elicits an asthmatic reaction (whether or not such a reaction includes a detectable IgE response).

Please replace the paragraph beginning on page 11 at line 1 with the following amended paragraph:

"Inducing agents": are compounds or other agents that induce a pAPC to produce stimulating cytokines. For example, if it is desired that a pAPC secrete Th1 stimulating cytokines, then factors such as LPS, CD40, CD40 ligand, BCGs, BCG oligonucleotides containing CpG motifs, TNF α , and microbial extracts such as preparations of *Staphylococcus aureus*, heat killed *Listeria*, modified cholera toxin, etc. can act as inducing agents ("Th1 inducing agents"). If instead it is desired that a pAPC secrete Th2 stimulating cytokines, then other factors (e.g., factors that induce IL-4 expression or inhibit IL-12 expression) can act as inducing agents ("Th2 inducing agents").

Please replace the paragraph beginning on page 13 at line 7 with the following amended paragraph:

Those of ordinary skill in the art will appreciate that the direction in which the Th1 vs Th2 response choice is to be influenced will depend upon the particular application in which the inventive techniques and reagents are being employed. Preferably, the inventive techniques and reagents are applied to allergic, asthmatic, or autoimmune disorders, as described more fully below.

Please replace the paragraph beginning on page 21 at line 10 with the following amended paragraph:

The cytokine(s) or inducing agent(s) to be administered is/are selected, of course, to reduce production of a Th1 or Th2 response, depending on the particular application involved, as discussed above. One preferred method of reducing a Th1 or Th2 response is through induction of the alternative response. Cytokines that, when expressed during antigen presentation to a T cell, induce a Th1 response in T cells (i.e., "Th1 stimulating cytokines") include IL-12, IL-2, IL-18, IL-1 β or fragments thereof, IFN α , and/or IFN γ , etc.; Th2 stimulating cytokines include IL-4. Inducing agents that prompt the expression of Th1

stimulating cytokines include factors such as LPS, CD40, CD40 ligand, ~~oligonucleotides~~
oligonucleotides containing CpG motifs, TNF α , and microbial extracts such as preparations
of *Staphylococcus aureus*, heat killed *Listeria*, and modified cholera toxin, etc.; inducing
agents that prompt the expression of Th2 stimulating cytokines include agents that induce IL-
4 expression by T cells or other cells, as well as agents that suppress IL-12 expression by
pAPC.

Please replace the paragraph beginning on page 23 at line 4 with the following amended
paragraph:

Coordinate control is particularly desirable where one or more of the cytokines,
inducing agents, or antigens being employed is a heterodimeric compound (e.g., IL-12). In
such cases, it will generally be desirable to express both ~~dimer~~ dimer components at
comparable levels, preferably under control of the same regulatory elements. Also, fusions
may be made with one or both ~~dimer~~ dimer components.

Please replace the paragraph beginning on page 26 at line 10 with the following amended
paragraph:

If desired, the dendritic cell phenotype may be confirmed using standard techniques
such as flow cytometry, or other approaches to detecting markers specific to dendritic cells
(see, for example, Example 6 5). Alternatively or additionally, flow cytometry or other
techniques may be used to isolate particular subsets of dendritic cells useful in accordance
with a relevant application of the present invention.

Please replace the paragraph beginning on page 35 at line 8 with the following amended paragraph:

Those of ordinary skill in the art will appreciate that any of a wide variety of assays may be employed to monitor the effects of inventive treatments described herein. For example, it may be desirable to assay the ability of *in vitro*-promulgated pAPCs to present antigen as desired, and/or to induce the desired response in helper T cells, prior to (or, in certain cases, instead of) introduction of the pAPCs into an individual or other system containing T cells. Any test may be used to accomplish such an assay; Examples 6-10 5-9 present certain preferred assays that could be used as tests to analyze the abilities and characteristics of *in vitro*-promulgated dendritic cells, and/or their appropriateness for administration to selected individuals.

Please replace the paragraph beginning on page 36 at line 1 with the following amended paragraph:

Dendritic cells are prepared from PBMC as described in Tøtting et al., (*J. Immunol.*, 160(3):1139-47, 1998) or Nestle et al., (*Nature Med.*, 4:328-32, 1998). PBMC are isolated from electrophoresed blood of healthy donors by density centrifugation on Ficoll-hypaque gradients (1.077 g/ml; LSM, Organon-Teknika, Durham, NC) for 20 min at 2000 rpm at room temperature. After four or five washes in HBSS (Life Technologies, Gaithersburg, MD) to remove platelets, cells are resuspended at 10^7 /ml in AIM-V medium (Life Technologies) and incubated for 1 h in 75-cm² tissue culture flasks (37°C, 5% CO₂). Nonadherent cells are gently washed out with HBSS and cryopreserved for use as T cell responders. The remaining plastic-adherent cells are further cultured (37°C, 5% CO₂) in AIM-v medium supplemented with 1000 U/ml rGM-CSF and 1000 U/rIL4 (Schering-Plough). After 7 to 10 days, nonadherent cells are harvested. DC generated in this way are 50 to 80% pure based on morphology and the expression of a CD3⁻, CD14⁻, CD16⁻, CD20⁻, CD40⁺, CD80⁺, CD86⁺, MHC class II⁺ immunophenotype as assessed by flow cytometry. Dendritic cells may also be purified further (>95%) by density gradient centrifugation.

Please replace the paragraph beginning on page 39 at line 20 with the following amended paragraph:

This assay measures cytokine secretion by primed cells. One million isolated PBMCs are stimulated with a specific antigen(s) (e.g. a peptide, protein or cellular lysate), and control protein for 48-72 hr. Supernatant is collected and analyzed for IFN- γ , IL-12, ~~IL-4~~ IL-4, and IL-5 by ~~enzyme-lined~~ enzyme-linked immunosorbent assay (ELISA; Endogen, Woburn, MA).